

Roxane Laboratories, Inc.

# IMPORTANT DRUG SAFETY INFORMATION Regarding Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL)

Dear Healthcare Professional:

Serious adverse events and deaths have resulted from accidental overdose of morphine sulfate oral solutions. In most of these cases, morphine sulfate oral solutions ordered in milligrams (mg) were mistakenly interchanged for milliliters (mL) of the product. When this occurs with a high concentration oral solution, such as Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL), the result is a 20-fold overdose. For example, a prescribed dose of 5 mg was mistakenly administered as 5 mL (100 mg) of the morphine sulfate concentrated solution. Other errors were a result of a lack of understanding of the concentration of morphine in the oral solution. Also, healthcare providers should read the instructions in the Medication Guide that describe the correct use of the oral syringe in order to help prevent medication errors from occurring, and should discuss the correct use of the oral syringe with patients. Information in this letter is intended to emphasize the importance of proper prescribing and dispensing of morphine sulfate oral solution, and to describe the newly available product labeling in order to help prevent medication errors.

In January 2010, the U.S. Food and Drug Administration (FDA) approved Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL) for relief of moderate to severe acute and chronic pain in opioid-tolerant patients. The approval of this product is part of FDA's unapproved drugs initiative. Prior to the recent approval, Roxane marketed a morphine sulfate oral solution with the strength expressed as 20 mg/mL, using a container label and carton labeling that had brown lettering on a white background. The newly approved product labeling and packaging feature revisions intended to reduce the risk of medication errors. Additionally, the new prescribing information also highlights the risk of medication errors with this product. These changes are described in detail below.

### **CARTON, CONTAINER, AND PACKAGING**

- The strength is presented as 100 mg per 5 mL followed by a less prominently displayed concentration of (20 mg/mL). The intent of this designation is to help differentiate this product from the 20 mg/5 mL morphine sulfate product.
- A bright yellow background is used on multiple sides of this product to differentiate the morphine sulfate oral solution 100 mg per 5 mL

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- (20 mg/mL) from other morphine sulfate oral solutions marketed by Roxane with a white background.
- The drug name, strength and concentration are displayed in white lettering on a red background as an additional means of differentiating this product from other concentrations of morphine sulfate oral solutions (see figures on pg 4 of this letter).
- A warning stating "ONLY FOR USE IN PATIENTS WHO ARE OPIOID TOLERANT" is displayed in a box to highlight that the morphine sulfate oral solution 100 mg per 5 mL (20 mg/mL) is indicated for use in opioid-tolerant patients only. The 100 mg per 5 mL concentration of morphine sulfate may cause fatal respiratory depression when administered to patients not previously exposed to opioids.
- A reminder is presented to the pharmacist to dispense the product to each patient with the enclosed Medication Guide.
- Both the 30 mL and 120 mL bottles of morphine sulfate 100 mg per 5 mL (20 mg/mL) oral solution are packaged with a calibrated oral syringe to provide accurate dose measurements. Healthcare providers should read the instructions in the Medication Guide that describe the correct use of the oral syringe in order to help prevent medication errors from occurring. Furthermore, healthcare providers should discuss the correct use of the oral syringe with their patients.

#### PRESCRIBING INFORMATION

- The prescribing information for this new product contains a boxed warning for risk of medication errors, where confusion between different concentrations and between "mg" and "mL" has resulted in accidental overdose and deaths.
- In addition, the risk of medication errors is also described in the "Indications and Usage," "Dosage and Administration" and "Warnings and Precautions" sections.
- A Medication Guide for the new product will be enclosed in the carton. This Medication Guide provides step-by-step directions and a pictogram to instruct patients on how to measure an accurate dose using the oral syringe as well as information pertaining to the associated risks of this medication, such as death from an overdose. The current package insert with medication guide is included with this letter.

## ENSURE THE PROPER DOSE OF MORPHINE SULFATE ORAL SOLUTION IS COMMUNICATED AND DISPENSED

Roxane currently distributes three morphine sulfate oral solutions:

- Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL); available in 30 mL and 120 mL bottles with calibrated oral dosing syringe.
- Morphine Sulfate Oral Solution 20 mg/5 mL; available in 100 mL and 500 mL bottles with graduated patient dispensing cup.
- Morphine Sulfate Oral Solution 10 mg/5 mL; available in 100 mL and 500 mL bottles with graduated patient dispensing cup. Additionally, a unit dose patient cup filled to deliver 5 mL (10 mg morphine sulfate) is available.

To assure that your patient receives the proper dose of morphine sulfate oral solution, please write a prescription for morphine sulfate oral solution clearly by including the following:



(1) The <u>concentration</u> of morphine sulfate oral solution (write out morphine sulfate and DO NOT use abbreviations) to be dispensed

#### **AND**

(2) The intended <u>dose</u> of morphine in milligrams (mg) with the corresponding <u>volume</u> in milliliters (mL) written out in the directions.

To demonstrate, a dose of 15 mg of morphine sulfate oral solution should be written as follows (depending on the concentration being prescribed):

Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL)

Sig: 15 mg (0.75 mL) orally every 4 hours prn.

Dispense: (indicate amount)

OR

Morphine Sulfate Oral Solution 20 mg/5 mL

Sig: 15 mg (3.75 mL) orally every 4 hours prn.

Dispense: (indicate amount)

OR

Morphine Sulfate Oral Solution 10 mg/5 mL

Sig: 15 mg (7.5 mL) orally every 4 hours prn.

Dispense: (indicate amount)

It is important that the prescription is filled with the proper concentration of morphine sulfate oral solution to prevent potential medication errors. **Please ensure the proper dose is communicated and dispensed.** If the specified morphine sulfate oral solution is unavailable, contact the prescriber.

Adverse events should be reported to Roxane Laboratories:

Mail: Roxane Laboratories, Inc. Phone 800-962-8364
Pharmacovigilance Department FAX 614-308-3540

P.O. Box 16532 Email dra-tpiwebsite@col.boehringer-ingelheim.com Columbus, OH 43216

You may also report adverse events directly to the FDA MedWatch Reporting System:

Mail: MedWatch Phone 800-332-1088 5600 Fishers Lane FAX 800-332-0178

Rockville, MD 20852-9787 On line <a href="www.fda.gov/medwatch/report.htm">www.fda.gov/medwatch/report.htm</a> (Please use the MedWatch Form 3500 available at: <a href="www.fda.gov/medwatch/getforms.htm">www.fda.gov/medwatch/getforms.htm</a>)

If you have any further questions or would like additional information, please contact our Technical Product Information Department at 1-800 962-8364 or <a href="https://www.roxane.com">www.roxane.com</a>.

Sincerely,

Roxane Laboratories, Inc.

Please see carton and container illustrations on page 4 of this letter



Figure 1. Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL), new *carton* label (30 mL carton shown for illustration)

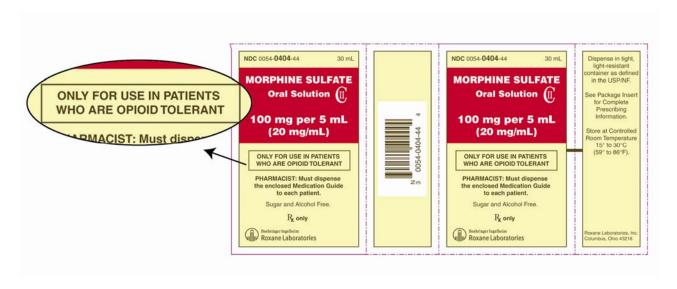


Figure 2. Morphine Sulfate Oral Solution 100 mg per 5 mL (20 mg/mL), new container label (120 mL container shown for illustration)



 $\underline{www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivities by FDA/SelectedEnforcementActions nsonUnapprovedDrugs/ucm118990.htm}$ 

<sup>&</sup>lt;sup>1</sup> US Food and Drug Administration. Unapproved drugs: drugs marketed in the United States that do not have required FDA approval. Accessed at:

<sup>&</sup>lt;sup>2</sup> Adapted from: Institute for Safe Medication Practices (ISMP). FDA Advise-ERR: A new look for Morphine Sulfate 100 mg per 5 mL (20 mg/mL) Oral Solution. *ISMP Medication Safety Alert!* 2010;15(3):1-2.